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ECBC memo dtd 27 Aug 2014

E.A.T.R. 120, COPY NO. 1.

TOXICITY OF CYANOGEN CHLORIDE TO WHITE MICE BY INHALATION.

By

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Forwarded to Chief, Chemical Warfare Service,

MAR 3 1933

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ABSTRACT

Object.

The object of this work was to provide accurate data on the toxicity of cyanogen chloride to white mice. The redetermination of this value was carried out under Project A 3 as one of the tests of a compound believed to have possibilities for development as a quick-acting nonpersistent agent. The new data also constitute a revision of the data on this important compound given in the summary of mouse toxicity data now being prepared (E.A.T.R. 109) under Project A 10.

Discussion.

Mice exposed to a lethal concentration of cyanogen chloride for 10 min. show, first, a period of excitement followed by quiet, then another period of excitement of very short duration followed immediately by convulsions and complete collapse. The median lethal concentration on mice for 10-min. exposures is twice as high as the median lethal concentration for phosgene and four times as high as the median lethal concentration of hydrocyanic acid gas for the same length of exposure on mice.

Conclusions.

The experimental lethal concentration on mice for 10-min. exposures is between 0.75 mg./l. and 0.781 mg./l. using a 24-hr. observation period.

The median lethal concentration, as read from the curve, for an exposure of 10 min. and an observation period of 24 hr. is 0.74 mg./l.

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TOXICITY OF CYANOGEN CHLORIDE TO WHITE MICE BY INHALATION.

I. INTRODUCTION.

The object of this work was to provide accurate data on the toxicity of cyanogen chloride to white mice. The redetermination of this value was carried out under Project A 3 as one of the tests of a compound believed to have possibilities for development as a quick-acting nonpersistent agent. The new data also constitute a revision of the data on this important compound given in the summary of mouse toxicity data now being prepared (E.A.T.R. 109) under Project A 10.

II. HISTORICAL.

Three different series of tests to determine the toxicity of cyanogen chloride to white mice for a 10-min. exposure were run at American University. A very small number of mice were used in each series and the results were extremely conflicting. In B.M. 12-47 the lethal concentration was estimated to be 0.2 mg./l., in B.M. 10-57 it was estimated to be 0.4 mg./l., and in P.R. 41 it was estimated to be 0.5 mg./l. By interpolation from data given in P.R. 222, the lethal concentration is about 0.64 mg./l.

III. THEORETICAL.

See E.A.T.R. 119 for a discussion of theoretical factors. The use of the term "median lethal concentration" to refer to the concentration required to kill 50% of a large group of animals exposed is continued in this report.

IV. EXPERIMENTAL.

A. Material.

1. Cyanogen Chloride.

The cyanogen chloride used (in cylinder 45739) was made at this Arsenal in May-June, 1932, for use in canister testing during development of the light-weight canister, Project D 1.1-24. A sample showed the following purity when analyzed by the Analytical Department of the Research Division:

Cyanogen chloride,	99.8%
Residue on evaporation,	none
Iron,	none
HCN,	0.06%

2. Animals Used.

The white mice used in these experiments were purchased from dealers. They ranged in weight from 18 to 30 g. They were in good condition. A lot of 100 were kept in observation cages for 30-day periods in order to check the normal death rate. The daily death rate, observed from the 23rd of November until the 12th of December (20 da.), was 0.65%.

B. Apparatus.

The apparatus used was the same as described in E.A.T.R. 119.

C. Procedure.

1. Operation of Apparatus.

Fully described in E.A.T.R. 119.

2. Distribution of Gas-Air Mixture.

The distribution of the gas-air mixture in the chamber is uniform (see E.A.T.R. 119).

3. The Method of Analysis.

In starting this work boiled sodium peroxide was used as the absorbent. Seventy-five cc. of 3% aqueous sodium peroxide was

placed in each petticoat bubbler. Two of these bubblers were connected in series and the gas-air sample was drawn through these bubblers at the rate of 3 l./min. for 10 min. An analysis of both bubblers at a concentration of 0.42 mg./l. showed that a better than 15% of this concentration was collected in the second bubbler. Checks at higher concentrations proved that some of the compound was passing into, if not through, a third bubbler.

The sulfite method was next tried (C.W.M. XXIV, Part I, p. 76) and later 2% sodium hydroxide in 75% alcohol was used as an absorbent. The sulfite method gave consistently about 1/2 of the concentration obtained either with the aqueous sodium peroxide or with the 2% sodium hydroxide (alcoholic) methods of absorbing the compound.

The Analytical Department was consulted at this stage of the investigation and at their suggestion the following method was used in collecting the concentration data found under section IV of this report.

Bead towers were used instead of petticoat bubblers. Twenty-five cc. of 6% solution of sodium hydroxide (aqueous), and 25 cc. of 95% alcohol, were placed in each bead tower. Check runs at high concentrations showed that two bead towers were ample to absorb all the cyanogen chloride at the concentrations used when the gas-air mixture was drawn through the bead towers for 10 min. at the rate of 2 l./min. The wet meter was used for measuring this flow through the bead towers. The analysis used was the Standard Volhard method for determining chlorides. The following formula was used in determining the concentration in milligrams per liter:

$$\frac{((\text{cc.}AgNO_3 \times \text{N.F.}) - (\text{cc.KSCN} \times \text{N.F.})) \times \text{Mol.wt. of CNCl}}{1000} \times \frac{1000}{\text{Vol.sample in liters}} = \text{mg. cyanogen chloride per liter.}$$

V. RESULTS.

In the following table are shown all the pertinent data collected in the individual toxicity experiments. Thirty cubic centimeters of silver nitrate (0.02008 N) were used in all tests. Capillary No. 5 was used throughout the tests.

Table 1.

Exposure of Mice to Cyanogen Chloride.

Run	Date	Concn.	Air temp.	Wet bulb	Rel. hum.	No. mice used	Mice dead at end of exposure	(0.00989) N KSCN	Diff. on flowmeter	Time to take air-gas samples
	1932	mg./l.	°F.	°F.	%			cc.	cm.	min. sec.
1	11/28	0.714	77	56	23	10	6	37.0*	20.5	10 1
2	11/28	0.720	77	56	23	20	6	36.8	20.5	10 15
3	11/28	0.747	76	55	22	20	7	35.9	20.6-21.6	10 5
4	11/29	0.808	75	54	21	20	13	33.9	26.4-27.0	10 3
5	11/29	0.781	75	54	21	20	10	34.8	27.0	10 2
6	11/30	0.892	74	59	29	20	14	31.15	33.3-33.4	9 54
7	11/30	0.945	73	56	32	20	19	29.4	40.8-41.1	10 13
8	11/30	0.604	79	58	25	20	2	40.6	19.3-19.4	9 53
9	11/30	0.553	79	58	25	20	3	42.3	16.3-16.2	10 9
10	11/30	0.358	78	56	21	20	0	48.7	9.7	10
11	12/1	0.489	76	63	51	20	0	44.4	10.4-10.2	10 5
12	12/1	0.458	72	58	42	20	2	45.4	11.6-11.5	10 1
13	12/1	0.429	73	57	35	20	1	46.4	9.8-10	10 8
14	12/1	0.748	72	56	34	20	15	36.3**	24.1	10 5
15	12/1	0.765	72	55	31	20	17	35.7**	24.3	10

* There was a blank of 0.006 mg./l. to subtract for the amount of caustic used in each bead tower.

**On runs 14 and 15 there was no blank to subtract for the amount of caustic used in each bead tower.

The dimensions of capillary No. 5 are: length, 7 cm., bore, 1/4 cm.

The following table is a rearrangement of the concentration data from Table 1 and the mortality data arranged in the decreasing order of concentrations for the purpose of showing more readily the method of arriving at the median lethal concentration.

Table 2.

Toxicity of Cyanogen Chloride to Mice.

Run	Concentration	No. of mice used	Deaths				Total deaths
			At end of exp.	24 hr.	5 da.	10 da.	
	mg./l.						
10	0.358	20	0	0	0	1	1
13	0.429	20	1	1	1	1	1
12	0.458	20	2	2	3	3	3
11	0.489	20	0	1	1	1	1
9	0.553	20	3	3	3	6	6
8	0.604	20	2	2	2	5	5
1	0.714	10	6	6	7	7	7
2	0.720	20	6	8	9	11	11
3	0.747	20	7	9	9	11	11
14	0.748	20	15	16	16	16	16
15	0.765	20	17	17	18	18	18
5	0.781	20	10	10	10	10	10
4	0.808	20	13	13	14	15	15
6	0.892	20	14	14	15	16	16
7	0.945	20	19	19	19	19	19

VI. DISCUSSION.

The effect noted during the gassing of the mice at lethal concentrations of cyanogen chloride followed very definite lines. During the first 3 min. of the exposure period the mice registered intense excitement. This was shown by a wild chasing around in the mouse container, indulged in by all the mice. At the end of the 3-min. interval there was a period of rest or quiet. Lacrimation could not be detected on the mice. This may have been due to limited observation. After 5 min., another period of excitement of short duration took place. At this time, the mice showed intense respiratory stimulation followed almost immediately by convulsions and complete collapse. During the last two to three minutes of the run, all the mice were down on the floor of the cage and did not move. At the end of the 10-min. run, when the cage was withdrawn from the gassing chamber (at a lethal concentration), 50% or more were dead. The rest showed complete collapse with respiration occurring at 1/2 to 1-min. intervals. A very few died in from 1 to 7 min. after removal from the gas. The remainder recovered very rapidly, getting on their feet in from 10 to 25 min. Of mice that so recovered, only 5 died subsequently during the first 24 hr.

The lethal concentration of cyanogen chloride for mice for 10-min. exposures is twice as high as that for phosgene (E.A.T.R. 119) and four times as high as that for hydrocyanic acid gas on mice for the same length of exposure (E.A.M.R.D. 20, p. 20).

VII. CONCLUSIONS.

The experimental lethal concentration of cyanogen chloride for mice for 10-min. exposures is between 0.75 mg./l. and 0.781 mg./l. using a 24-hr. observation period.

The median lethal concentration, as read from the curve, for an exposure of 10 min. and an observation period of 24 hr., is 0.74 mg./l.

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Work started: Nov. 15, 1932.
Work completed: Dec. 10, 1932.

Toxicity of Cyanogen Chloride to White Mice by Inhalation.

E.A.T.R. 120.

Project A 10.2.

8 copies made)
Typed - mcc)

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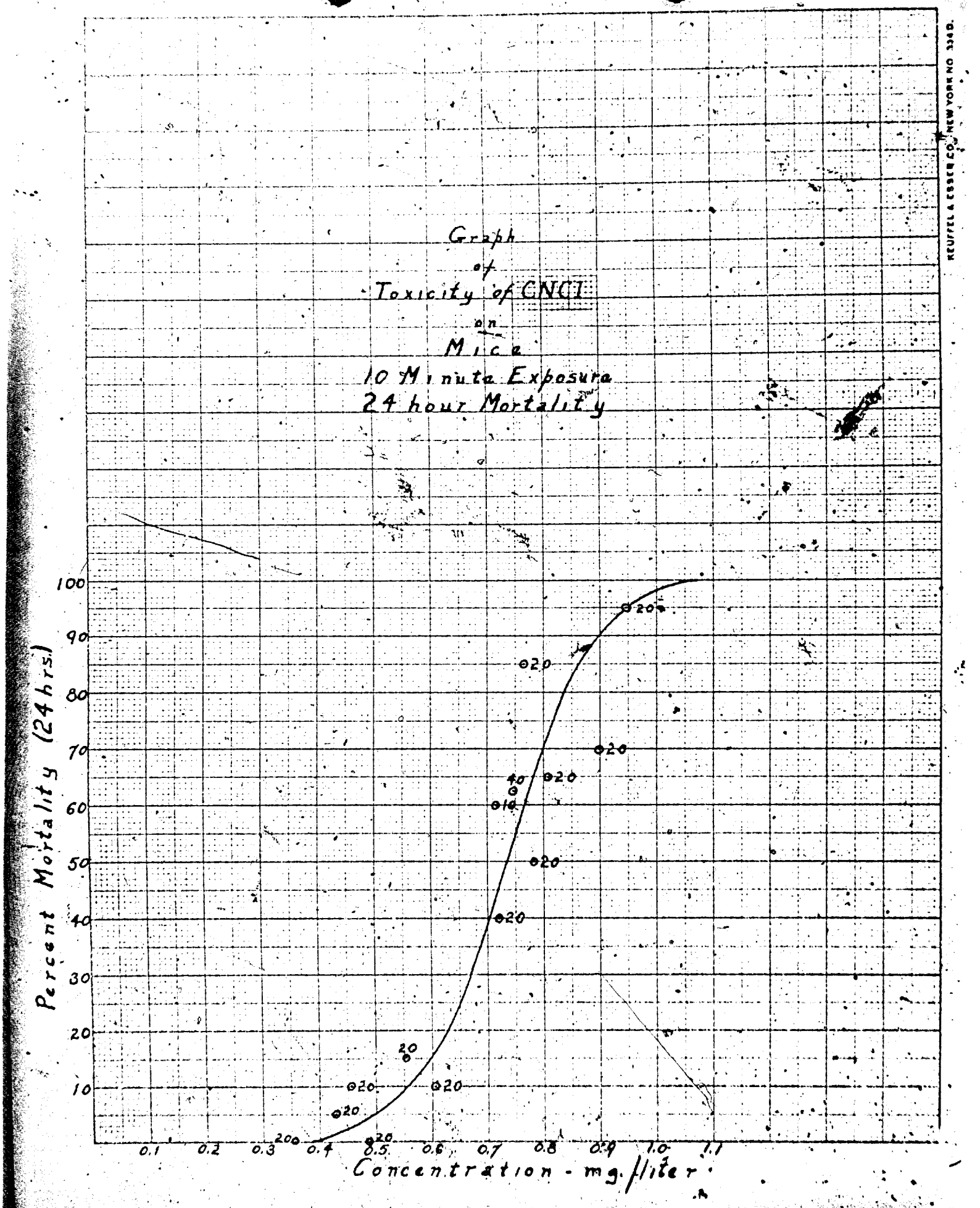
Graph
of
Toxicity of CNCl
on
Mice
10 Minute Exposure
24 hour Mortality
Percent Mortality (24 hrs.)
100
90
80
70
60
50
40
30
20
10
0.1
0.2
0.3
0.4
0.5
0.6
0.7
0.8
0.9
1.0
1.1
Concentration - mg./liter
20
40
10
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FOR Defense Technical Information Center, 8725 John J. Kingman Road, Ft Belvoir, VA 22060

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1. This action is in response to an Edgewood Chemical Biological Center (ECBC) Internal Request for a Change in Distribution on documents related to cyanogen chloride.

2. The listed documents in the attachment have been reviewed by ECBC Subject Matter Experts and deemed suitable for the change in distribution to read "Approved for Public Release; distribution unlimited."

3. The point of contact is Adana L. Eilo, ECBC Security Specialist, (410) 436-2063, adana.l.eilo.civ@mail.mil.

Encl

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Security Manager

Cyanogen Chloride References

[1] Armstrong, GC, *Toxicity of Cyanogen Chloride to White Mice by Inhalation,* War Department, Chemical Warfare Service, Edgewood Arsenal, MD, 03 March 1933. Unclassified, Dist. D. DoD/Contractors. AD# B956466.

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